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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/723,250	11/26/2003	Thomas M. DiMauro	3518.1024-000	6059

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EXAMINER	
HUYNH, CARLIC K	

ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
11/28/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/723,250	DIMAURO ET AL.	
	Examiner	Art Unit	
	Carlic K. Huynh	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-25 and 27-89* is/are pending in the application.

4a) Of the above claim(s) *11-20,31-59,61-69 and 71-88* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-10,21-24,26-30,60,70 and 89* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :18 May 2007 and 15 October 2007.

DETAILED ACTION

Receipt of Applicants' amendments and remarks filed on September 4, 2007 is acknowledged.

Status of the Claims

1. Claims 1-5, 7-25, and 27-89 are pending in the application, with claims 6 and 26 having been cancelled, in an "Amendment – After Non-Final Rejection" on September 4, 2007. It is noted that claims 11-20, 31-59, 61-69, and 71-88 have been withdrawn in a Response to Election / Restriction filed on March 23, 2007. Accordingly, claims 1-5, 7-10, 21-25, 27-30, 60, 70, and 89 are being examined on the merits herein.

Information Disclosure Statement

The Information Disclosure Statements submitted on May 18, 2007 and October 15, 2007 are acknowledged.

Response to Arguments

2. Applicant's arguments, see "Amendment-After Non-Final Rejection" filed on September 4, 2007, with respect to "Amendments to the Specification" to the use of trademarks in the specification have been fully considered and are found. Applicants have argued that all trademarks listed with the specification do comply with the requirements. The trademarks used in the specification do comply with the requirements as the trademarks are capitalized and are

accompanied by the generic terminology. Thus, the Objection to the Specification for use of trademarks in the specification has been withdrawn in light of the arguments.

3. Applicant's arguments, see "Amendment-After Non-Final Rejection" filed on September 4, 2007, with respect to "Rejections under 35 U.S.C. § 102(b)" to claim 60 have been fully considered and are found persuasive. Applicants argue that Trieu (US 2002/0026244) does not **explicitly** teach a device that is inserted into the vertebral body adjacent to the vertebral disc. Examiner agrees with Applicants' arguments. Thus, the Rejections under 35 U.S.C. § 102(b) to claim 60 has been withdrawn in light of the arguments.

4. Applicant's arguments, see "Amendment-After Non-Final Rejection" filed on September 4, 2007, with respect to "Rejections under 35 U.S.C. § 103" to claims 1-10, 21-30, 70, and 89 has been fully considered and are not found persuasive. It is noted applicants have cancelled claims 6 and 26 and amended claims 1, 70, and 89 to recite "wherein the anti-resorptive agent is a highly specific cytokine antagonist that inhibits TNF-α".

Applicants argue that Radomsky (US 5,942,499) does not teach local administration of a bone forming agent and administration of a highly specific cytokine antagonist that inhibits TNF-α. Applicants further argue that Boyle et al. (US 2003/0207827) does not teach the local administration of a highly specific cytokine antagonist that inhibits TNF-α. Moreover, applicants argue that both references in combination do not teach local administration of a bone forming agent and administration of a highly specific cytokine antagonist that inhibits TNF-α.

Radomsky does teach the administration to the desired site of bone growth such as vertebral compression fractures for the treatment of osteoporosis (column 2, lines 50, 54, and 57). It would be obvious the "desired site of bone growth" may be adjacent to the bone in the

vertebral body. Boyle et al. teaches a method of treating osteoporosis comprising administering osteoprotegerin, which inhibits the TNF family of receptors (page 4, paragraph [0043]). Since TNF-α is a known member of the TNF family, it would be obvious that osteoprotegerin inhibits TNF-α. Boyle et al. further teaches that estrogen is a known antiresorptive agent (page 41, paragraph [0355]). Thus, there is sufficient evidence in both references to teach the local administration of a bone forming agent and administration of a highly specific cytokine antagonist that inhibits TNF-α.

Thus, the Rejections under 35 U.S.C. § 103 to claims 1-10, 21-30, 70, and 89 remain rejected.

5. Applicant's arguments with respect to claims 1-10, 21-30, 60, 70, and 89 have been considered but are moot in view of the new ground(s) of rejection. The following new ground(s) of rejection to amended claims 1-5, 7-10, 21-25, 27-30, 60, 70, and 89 are used herewith.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claim 60 is rejected under 35 U.S.C. 103(a) as being unpatentable over Trieu et al. (US 2002/0026244).

Trieu teaches methods of implanting nucleus pulposus implants (page 1, paragraph [0007]). The method involves removal of the natural nucleus pulposus of the intravertebral disc and implantation of the nucleus pulposus of the invention (page 10, paragraph [0109]). The nucleus pulposus implant of the invention may contain pharmacological agents used to treat osteoporosis including a bone morphogenetic protein, growth factors such as fibroblast growth factor and platelet-derived growth factor, and steroids (page 9, paragraphs [0101] and [0104]). It would be obvious the bone forming agent may be a bone morphogenetic protein and the steroid is estrogen. It would be obvious the implant may be between an upper vertebral body and a lower vertebral body within the vertebral disc or adjacent to the vertebral disc that can release the pharmacological agent to the bone since Trieu teaches disc space utilizing devices known in the art (page 10, paragraph [0109]).

7. Claims 1-10, 21-30, 70, and 89 is rejected under 35 U.S.C. 103(a) as being unpatentable over Radomsky (US 5,942,499) in view of Trieu et al. (US 2002/0026244) and Boyle et al. (US 2003/0207827).

Radomsky teaches a bone growth-promoting composition comprising growth factors such as fibroblast growth factor and platelet-derived growth factor and their methods of use (column 1, lines 19, 35-36, and 61). The invention can be used in various sites of desired bone growth including vertebral compression fractures and in pathological bone defects associated with osteoporosis (column 2, lines 50 and 55-58). The invention describes an injectable mixture of growth factor for intraosseous, or within bone, administration (column 12, lines 5-12).

Radomsky does not teach an anti-resorptive agent, a hip bone, an intact bone, and local administration to bones that is adjacent to the bone.

Trieu teaches methods of implanting nucleus pulposus implants (page 1, paragraph [0007]). The method involves removal of the natural nucleus pulposus of the intravertebral disc and implantation of the nucleus pulposus of the invention (page 10, paragraph [0109]). The nucleus pulposus implant of the invention may contain pharmacological agents used to treat osteoporosis including a bone morphogenetic protein, growth factors such as fibroblast growth factor and platelet-derived growth factor, and steroids (page 9, paragraphs [0101] and [0104]). The device of Trieu is placed adjacent to unfractured bones (page 9, paragraphs [0104]). Since the nucleus pulposus implant of the invention may contain pharmacological agents used to treat osteoporosis including a bone morphogenetic protein (see page 9, paragraph [0101]), it would be obvious that the device can be used to treated fractured bones such as a hip bone. Thus Trieu teaches local administration in between bones.

Boyle et al. teach methods to treat bone diseases such as osteoporosis comprising osteoprotegrin, which is a polypeptide that plays a role in promoting bone accumulation (page 1, paragraphs [0001] and [0006]). Boyle et al. further teach treatment of osteoporosis in postmenopausal women and a direct relationship between osteoporosis and incidence of hip and neck fractures (page 9, paragraph [0095]). Osteoprotegrin acts as a receptor of the TNF family and prevents receptor-ligand interaction (page 4, paragraph [0043]). Osteoprotegrin also blocks interleukin (IL)1-α and IL1-β produced hypercalcemia (page 40, paragraph [0344]). Boyle et al. also teaches that estrogen is a known antiresorptive agent (page 41, paragraph [0355]).

Accordingly, absence the showing of unexpected results, it would have been obvious to a person of skill in the art at the time of the invention to employ the methods of promoting bone growth comprising a growth factor of Randomsky to be locally administered in between bones

and with an anti-resorptive agent on hip bones because the device of Trieu teach a device for local administration in between bones and Boyle et al. teach the anti-resorptive agent osteoprotegrin as well as treatment of osteoporosis on various bones such as the hip bone and according to Trieu, a device to deliver agents in between bones can be used to treat osteoporosis and according to Boyle et al., osteoprotegrin can be used to treat osteoporosis in various bones such as the hip.

The motivation to combine the methods of Radomsky to the methods of Treiu and Boyle et al. is that the methods of Trieu can be used for local administration in between bones to treat osteoporosis and the methods of Boyle et al. teach osteoprotegerin can be used to treat osteoporosis in various bones including the hip bone.

It is noted that "It is obvious to combine individual compositions taught to have the same utility to form a new composition for the very same purpose" and "It is obvious to combine two compositions taught by the prior art to be useful for the same purpose to form a third composition that is to be used for the very same purpose". *In re Kerkhoven*, 626 F.2d 846, 205 U.S.P.Q. 1069 (C.C.P.A. 1980).

Regarding post-menopausal as recited in claims 4 and 24, it is well known in the art that osteoporosis affects mainly elderly females. Thus, it would be obvious the patient population is post-menopausal.

Conclusion

8. No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carlic K. Huynh whose telephone number is 571-272-5574. The examiner can normally be reached on Monday to Friday, 8:30AM to 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

S. Wang

ckh

SHENGJUN WANG
PRIMARY EXAMINER